

**Appln No. 09/927,779**  
**Amdt date November 30, 2004**  
**Reply to Office action of November 1, 2004**

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) A molecular detector for detecting single-molecules in solution comprising:  
a solution reservoir;  
at least one biofunctionalized nanometer-scale mechanical resonator disposed within the reservoir;  
a detector in signal communication with the at least one resonator for measuring the mechanical displacement of the resonator.
2. (Original) A molecular detector as described in claim 1, wherein the at least one resonator comprises a resonator selected from the group consisting of: vibrational resonators, rotational resonators, torsional resonators and composite resonators.
3. (Original) A molecular detector as described in claim 1, wherein the at least one resonator is a notched vibrational cantilever.
4. (Original) A molecular detector as described in claim 1, wherein the at least one resonator is biofunctionalized with a receptor.
5. (Original) A molecular detector as described in claim 4, further comprising a substrate disposed within the reservoir and adjacent to the at least one resonator, wherein the substrate is biofunctionalized with a ligand capable of molecular interaction with the receptor.
6. (Original) A molecular detector as described in claim 4, further comprising a substrate disposed within the reservoir and adjacent to the at least one resonator, wherein the substrate is

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biofunctionalized with a receptor capable of molecular interaction with a ligand wherein the ligand is capable of molecular interaction with the receptor on the resonator.

7. (Original) A molecular detector as described in claim 1, comprising at least two resonators arranged adjacent to one another, wherein at least one of the resonators is biofunctionalized with a receptor to form a receptor resonator and at least one of the resonators adjacent to the receptor resonator is biofunctionalized with a ligand capable of molecular interaction with the receptor.

8. (Original) A molecular detector as described in claim 1, comprising at least two resonators arranged adjacent to one another, wherein at least one of the resonators is a driver resonator comprising a driving element capable of mechanically displacing the driver resonator at a chosen frequency, wherein the driver resonator is biofunctionalized with a receptor; and  
at least one of the resonators adjacent to the driver resonator is biofunctionalized with a ligand capable of molecular interaction with the receptor on the driver resonator.

9. (Original) A molecular detector as described in claim 1, comprising at least three resonators arranged adjacent to one another, wherein at least one of the resonators is a driver resonator comprising a driving element capable of mechanically displacing the first driver resonator at a chosen frequency;

wherein at least one of the resonators is a second driver resonator comprising a driving element capable of mechanically displacing the second driver resonator at a chosen frequency; and

at least one of the resonators is a follower resonator disposed between the two driver resonators and biofunctionalized with a ligand; wherein the driver resonators are driven in antiphase, and wherein at least one of the driver resonators is biofunctionalized with a receptor capable of molecular interaction with the ligand on the follower resonator.

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10. (Original) A molecular detector as described in claim 8 or 9 wherein the driver is a piezoelectric device.

11. (Original) A molecular detector as described in claim 1, wherein the at least one resonator is made from a material selected from the group consisting of: silicon oxide, silicon, silicon carbide and gallium arsenide.

12. (Original) A molecular detector as described in claim 1, wherein the detector is integral with the resonator.

13. (Original) A molecular detector as described in claim 1, wherein the detector is a piezoresistive transducer.

14. (Original) A molecular detector as described in claim 13, wherein the transducer is made of p+ doped silicon.

15. (Original) A molecular detector as described in claim 1, wherein the detector is an optical detector.

16. (Original) A molecular detector as described in claim 1, wherein the detector is a lock-in detector.

17. (Original) A molecular detector as described in claim 1, wherein the resonator has a thickness between about 10nm and 1 $\mu$ m, a width between about 10nm and 1 $\mu$ m, and a length between about 1 $\mu$ m and 10  $\mu$ m.

18. (Original) A molecular detector as described in claim 1, wherein the resonator has a resonance motion vacuum frequency between about 0.1 and 12MHz.

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19. (Original) A molecular detector as described in claim 1, wherein the resonator has a force constant between about 0.1mN/m and 1 N/m.
20. (Original) A molecular detector as described in claim 1, wherein the resonator has a Reynolds number between about 0.001 and 2.0.
21. (Original) A molecular detector as described in claim 1, wherein the resonator has a mass loading coefficient between about 0.3 and 11.
22. (Original) A molecular detector as described in claim 1, having a force sensitivity of about 8fN/Hz or greater.
23. (Original) A molecular detector as described in claim 1, biofunctionalized to detect a receptor/ligand interaction.
24. (Original) A molecular detector as described in claim 1, biofunctionalized to detect DNA hybridization.
25. (Original) A molecular detector as described in claim 1, biofunctionalized to detect a chemical bond.
26. (Original) A molecular detector as described in claim 1, biofunctionalized to detect protein unfolding.
27. (Withdrawn) A molecular detector system comprising:  
at least one microfluidic channel;

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at least one array of molecular detector devices disposed within the at least one microfluidic channel, wherein the at least one array comprises a plurality of biofunctionalized nanometer-scale mechanical resonators each resonator having at least one detector in signal communication therewith for measuring the resonance motion of the resonator.

28. (Withdrawn) A molecular detector system as described in claim 27, wherein the plurality of resonators has at least two different biofunctionalizations.

29. (Withdrawn) A method for forming a molecular detector comprising:

supplying a substrate;

depositing a photoresist on the substrate;

exposing a pattern comprising the resonator on the photoresist;

etching the substrate to form the resonator; and

removing the photoresist.

30. (Withdrawn) The method according to claim 29 wherein the pattern is formed by direct write e-beam lithography.

31. (Withdrawn) A method of detecting a molecule of interest comprising the steps of:

providing a molecular detector comprising a biofunctionalized nano-scale resonator adapted to move in response to the thermal motion of a solution, the molecular detector further comprising a detector disposed thereon, the detector being designed to monitor the mechanical displacement of the resonator;

placing the molecular detector into a solution such that the resonator is mechanically displaced based on the thermal motion of the solution and such that in the presence of a species capable of molecular interaction with the biofunctionalized resonator, the mechanical displacement of the resonator is altered; and

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measuring the mechanical displacement of the resonator such that a change in the mechanical displacement of the resonator is communicated to a user.

32. (Withdrawn) A method of detecting a molecule of interest comprising utilizing a molecular detector according to claim 1.